

WHAT IS CLAIMED IS:

- 1 1. A method of inducing apoptosis in a cancer cell, the method
2 comprising contacting the cell with:
 - 3 i. an anti-DR4 or anti-DR5 affinity agent agonist; and
 - 4 ii. an apoptosis-inducing agent.
- 1 2. The method of claim 1, wherein the agonist is an anti-DR-5 antibody.
- 1 3. The method of claim 2, wherein the anti-DR5 antibody has the binding
2 specificity of an antibody comprising a heavy chain variable region comprising the sequence
3 displayed in Figure 24 or Figure 35 and a light chain variable region as displayed in Figure
4 25 or Figure 35.
- 1 4. The method of claim 3, wherein the anti-DR5 antibody comprises a
2 heavy chain variable region comprising the sequence displayed in Figure 24 or Figure 35 and
3 a light chain variable region as displayed in Figure 25 or Figure 35.
- 1 5. The method of claim 2, wherein the anti-DR5 antibody is Antibody A
2 (ATCC Deposit No. ____).
- ✓ 1 6. The method of claim 1, wherein the agonist is an anti-DR4 antibody.
- 1 7. The method of claim 1, wherein the cell is contacted with an anti-DR4
2 antibody agonist and an anti-DR5 antibody agonist.
- 1 8. The method of claim 1, wherein the agonist is a humanized antibody.
- 1 9. The method of claim 1, wherein the agonist is a single chain antibody.
- 1 10. The method of claim 1, wherein the agent prevents or reduces the
2 expression of BCL-2.
- 1 11. The method of claim 10, wherein the agent prevents activation of
2 NFκB.
- 1 12. The method of claim 11, wherein the agent prevents degradation of
2 IκB.

- 1 13. The method of claim 1, wherein the agent is a proteasome inhibitor.
- 1 14. The method of claim 13, wherein the proteasome inhibitor is selected
2 from the group consisting of PS-341, MG-262 and MG-132.
- 1 15. The method of claim 1, wherein the agent is an inhibitor of an Inhibitor
2 of Apoptosis (IAP) protein.
- 1 16. The method of claim 15, wherein the inhibitor is SMAC or a SMAC
2 mimetic.
- 1 17. The method of claim 1, wherein the cancer cell is a colon cancer cell or
2 a pancreatic cancer cell.
- 1 18. The method of claim 1, wherein the agent is an antagonist of PAK1.
- 1 19. The method of claim 1, wherein the agent is an antagonist of a
2 polypeptide selected from the group consisting of nsurf and JIK.
- 1 20. The method of claim 1, wherein the agent is a siRNA.
- 1 21. A method of inducing apoptosis in a cancer cell in an individual in
2 need thereof, the method comprising,
3 administering to the individual a therapeutically effective amount of
4 i. an anti-DR4 or anti-DR5 affinity agent agonist; and
5 ii. an apoptosis-inducing agent.
- 1 22. The method of claim 21, wherein the agonist and the agent are
2 administered separately.
- 1 23. The method of claim 21, wherein the agonist and the agent are
2 administered as a mixture.
- 1 24. The method of claim 21, wherein the agonist is an anti-DR-5 antibody.
- 1 25. The method of claim 24, wherein the anti-DR5 antibody has the
2 binding specificity of an antibody comprising a heavy chain variable region comprising the

3 sequence displayed in Figure 24 or Figure 35 and a light chain variable region as displayed in
4 Figure 25 or Figure 35.

1 26. The method of claim 25, wherein the anti-DR5 antibody comprises a
2 heavy chain variable region comprising the sequence displayed in Figure 24 or Figure 35 and
3 a light chain variable region as displayed in Figure 25 or Figure 35.

1 27. The method of claim 25, wherein the anti-DR5 antibody is Antibody A
2 (ATCC Deposit No. _____).

1 28. The method of claim 21, wherein the agonist is an anti-DR4 antibody.

1 29. The method of claim 21, wherein the cell is contacted with an anti-
2 DR4 antibody agonist and an anti-DR5 antibody agonist.

1 30. The method of claim 21, wherein the agonist is a humanized antibody.

1 31. The method of claim 21, wherein the agonist is a single chain antibody.

1 32. The method of claim 21, wherein the agent prevents or reduces the
2 expression of BCL-2 or Ubch10.

1 33. The method of claim 32, wherein the agent prevents activation of
2 NF κ B.

1 34. The method of claim 33, wherein the agent prevents degradation of
2 I κ B.

1 35. The method of claim 21, wherein the agent is a proteasome inhibitor.

1 36. The method of claim 35, wherein the proteasome inhibitor is selected
2 from the group consisting of PS-341, MG-262 and MG-132.

1 37. The method of claim 21, wherein the agent is an inhibitor of an
2 Inhibitor of Apoptosis (IAP) protein.

1 38. The method of claim 37, wherein the inhibitor is SMAC or a SMAC
2 mimetic.

1 39. The method of claim 21, wherein the cancer cell is a colon cancer cell
2 or a pancreatic cancer cell.

1 40. The method of claim 21, wherein the agent is an antagonist of PAK1.

1 41. The method of claim 21, wherein the agent is an antagonist of a
2 polypeptide selected from the group consisting of UbcH10, nsurf and JIK.

1 42. The method of claim 21, wherein the agent is a siRNA.

1 43. A physiological composition comprising, a therapeutically effective
2 amount of

3 i. an anti-DR4 or anti-DR5 affinity agent agonist; and

4 ii. an apoptosis-inducing agent.

1 44. The physiological composition of claim 43, wherein the agonist is an
2 anti-DR-5 antibody.

1 45. The physiological composition of claim 44, wherein the anti-DR5
2 antibody has the binding specificity of an antibody comprising a heavy chain variable region
3 comprising the sequence displayed in Figure 24 or Figure 35 and a light chain variable region
4 as displayed in Figure 25 or Figure 35.

1 46. The physiological composition of claim 45, wherein the anti-DR5
2 antibody comprises a heavy chain variable region comprising the sequence displayed in
3 Figure 24 or Figure 35 and a light chain variable region as displayed in Figure 25 or Figure
4 35.

1 47. The physiological composition of claim 46, wherein the anti-DR5
2 antibody is Antibody A (ATCC Deposit No. ____).

1 48. The physiological composition of claim 43, wherein the agonist is an
2 anti-DR4 antibody.

1 49. The physiological composition of claim 43, wherein the cell is
2 contacted with an anti-DR4 antibody agonist and an anti-DR5 antibody agonist.

- 1 50. The physiological composition of claim 43, wherein the agonist is a
2 humanized antibody.
- 1 51. The physiological composition of claim 43, wherein the agonist is a
2 single chain antibody.
- 1 52. The physiological composition of claim 43, wherein the agent prevents
2 or reduces the expression of BCL-2 or UbcH10.
- 1 53. The physiological composition of claim 52, wherein the agent prevents
2 activation of NFκB.
- 1 54. The physiological composition of claim 53, wherein the agent prevents
2 degradation of IκB.
- 1 55. The physiological composition of claim 43, wherein the agent is a
2 proteasome inhibitor.
- 1 56. The physiological composition of claim 43, wherein the agent is an
2 inhibitor of an Inhibitor of Apoptosis (IAP) protein.
- 1 57. The physiological composition of claim 56, wherein the inhibitor is
2 SMAC or a SMAC mimetic.
- 1 58. The physiological composition of claim 43, wherein the agent is an
2 antagonist of PAK1.
- 1 59. The physiological composition of claim 43, wherein the agent is an
2 antagonist of a polypeptide selected from the group consisting of UbcH10, nsurf and JIK.
- 1 60. The physiological composition of claim 43, wherein the agent is a
2 siRNA.
- 1 61. An affinity agent with the binding specificity of an antibody
2 comprising a heavy chain variable region comprising the sequence displayed in Figure 24 or
3 Figure 35 and a light chain variable region as displayed in Figure 25 or Figure 35.

1 62. The affinity agent of claim 62, which is an antibody comprising a
2 heavy chain variable region comprising the sequence displayed in Figure 24 or Figure 35 and
3 a light chain variable region as displayed in Figure 25 or Figure 35.

1 63. A cell that expresses the antibody of claim 62.

1 64. A method of inducing apoptosis in a cancer cell, the method
2 comprising contacting the cell with an affinity agent with the binding specificity of an
3 antibody comprising a heavy chain variable region comprising the sequence displayed in
4 Figure 24 or Figure 35 and a light chain variable region as displayed in Figure 25 or Figure
5 35.